REMARKS

The Applicant hereby submits the present *Request For Reconsideration* in response to the Final Office Action mailed on 15 June 2005.

Claims 1-3, 5-17, and 19-28 are pending in the present application and finally rejected by the Final Office Action mailed on 15 June 2005. In the present Request for Reconsideration, the Applicant does not amend or cancel any of pending claims 1-3, 5-17, and 19-28.

Based on the reasons provided herein, the Applicant submits that all pending claims 1-3, 5-17, and 19-28 meet all requirements under the patent laws and are novel and non-obvious over the prior art of record. The Applicant respectfully requests the Examiner to reconsider the positions taken in the Final Office Action based on these reasons and to allow the present application as appropriate.

In the Final Office Action mailed on 15 June 2005, the Examiner rejected claims 1-3, 5-17, and 19-28 under 35 U.S.C. § 112, second paragraph. In the rejection, the Examiner states that claims 1 and 15 are unclear, specifically arguing that it is unclear whether the "gene sequence" or the "gene family data" are "stored in a file."

In response, the Applicant respectfully submits that claims 1 and 15 are clear to one ordinarily skilled in the art as written. Claims 1 and 15 specifically recite the term "gene family data" to express *data* and the term "gene sequence" to express a gene sequence. It is clear to one ordinarily skilled in the art reading these claims that *gene family data* are stored in a file, but a gene sequence associated with such data would not be stored in the file. For further clarification, the claim also explicitly recites "gene sequence data corresponding to a gene sequence" which distinguishes between the gene sequence and gene sequence data. As apparent, it is clear that claims 1 and 15 mean that

gene family data are stored in the file with use of the phrase "gene family data of the gene sequence stored in a file."

The specification is also consistent with the interpretation that the gene family data are stored in a file to implement the primer selection rules. See e.g. the application on page 41 at lines 3-5: "[t]he primerout file lists candidate primer sequences that otherwise met the primer selection rules, but was found in one of the *gene family files* and was therefore rejected"; and on page 33 at lines 10-14: "[t]hus, the software can select primers that are unique to the gene of interest and can be relied upon for genes that are members of families. This functionality can be added to the functionality of picking the best primers around the exons of a gene for the primer design process – select the candidate primer only if it is unique to the target file and *not present in the gene family files*").

Note further that the term "prestored gene family data" was previously amended to "gene family data of the gene sequence stored in a file" to satisfy a previous rejection of claims 1 and 15 by the Examiner. Thus, it is also clear from the prosecution history that it is the *gene family data* that are stored in a file.

Thus, the Applicant submits that claims 1-3, 5-17, and 19-28 are not indefinite under 35 U.S.C. § 112, second paragraph, and respectfully request the Examiner to withdraw such rejections. Since dependent claims 2, 3, 16, and 17 have no further rejections, each of these claims 2, 3, 16, and 17 is allowable over the prior art of record without further argument.

In the same Office Action, the Examiner maintained the rejection of claims 1 and 5-8 under 35 U.S.C. § 102(b) as being anticipated by Hwang et al. Specifically, the Examiner responds to three (3) points made by the Applicant in the previous Amendment and Request for Reconsideration. The Applicant now responds to each one of the responses made by the Examiner.

The standard for invalidity for anticipation from the prior art is well-established. "A prior art reference anticipates a patent claim if the reference discloses, either expressly

or inherently, all of the limitations of the claim." EMI Group N. Am., Inc. v. Cypress Semiconductor Corp., 268 F.3d 1342, 1350 (Fed. Cir. 2001) (citations omitted). The Applicant respectfully submits that the prior art described in the publication cited by the Examiner does not teach a computer-implemented method of processing gene sequence data comprising all the limitations of the pending claims.

(1) In the Examiner's continued rejection, the Examiner discusses Hwang et al. as utilizing "any particular annealing temperature" for teaching the limitations of claims 1 and 15. In response, the Applicant respectfully disagrees with the Examiner's interpretation and rejection of claims 1 and 15 and submits that all pending claims are allowable for the following reasons.

The claims specifically recite that "the set of primer selection rules [include] a first rule specifying that the primer pair data for the coding sequence be obtained *for a predetermined annealing temperature*", with the additional steps of "repeating the acts of identifying and storing such that primer pair data are obtained for each coding sequence of the plurality of coding sequences *at the predetermined annealing temperature*", as well as the step of "simultaneously amplifying the plurality of coding sequences in gene sequences from three or more individuals *at the predetermined annealing temperature* using the identified pairs of primer sequences."

Given the above-recited claim limitations written with a deliberate use of proper antecedent basis, it is clear that the only broadest reasonable interpretation of the claims 1 and 15 is that the same predetermined annealing temperature is utilized in the repeated identification of primer sequences and final simultaneous amplification. In contrast, Hwang et al. teach or suggest no computer process that utilizes the same predetermined annealing temperature for the identification of primer pair data for each coding region of the plurality of coding sequences and final simultaneous amplification thereof at the predetermined annealing temperature.

The claims must be interpreted in light of the teachings in the specification. In the present case, the specification is inconsistent with the Examiner's interpretation but

consistent with the Applicant's. The correct interpretation of the steps associated with "predetermined annealing temperature" is that the same predetermined annealing temperature is utilized for every iteration of the computer process. See e.g. page 11 at lines 10-14: "For example, the primer selection rules may include a rule specifying that all primer pair data for the plurality of coding regions be obtained for a single predetermined annealing temperature (e.g., 62° Celsius). This rule allows for the subsequent simultaneous amplification of many sequences in a single amplification run at the predetermined annealing temperature"; and on page 42 at lines 8-10: "It is more efficient to do simultaneous amplifications of four or five regions in 500 people, for example, rather than doing them one by one. This is where the rule regarding the fixed predetermined annealing temperature (e.g., 62° Celsius) comes into play: since all of the primers selected by the program having the same annealing temperature, the work can be done more efficiently"). Hwang et al. do not remotely teach or suggest any such computer-implemented rule that specifies such a predetermined annealing temperature for each coding sequence as claimed.

For the reasons in (1) alone, Hwang et al. do not teach or suggest the invention as claimed and the Examiner's continued § 102(b) rejection should be withdrawn.

Further, in the previous Office Action of 3 November 2004, the Examiner directed the Applicant's attention to p. 3346 at col. 2 and p. 3349 at the paragraph bridging cols. 1-2, which does not teach or suggest what is claimed. The Applicant submits that the last paragraph of the methods section of Hwang et al. describes a type of standard experimental protocol for expansion of cDNA using the polymerase chain reaction (PCR). Applicant acknowledges that the PCR protocol which the authors followed specifies certain set temperatures for denaturation, for annealing, and for expression of the sample cDNA. The authors specify certain time duration intervals for the several serial reaction phases within each PCR round or cycle, and specify a certain number of cycles for the PCR protocol. In addition, the authors specified certain defined oligonucleotide sequences for their three constructed primer pairs.

Based on the above, however, it cannot be inferred that the authors had intended to specify their oligonucleotide sequences on the basis of any particular annealing temperature. To the contrary, their intention in specifying the sequences of their constructed primer pairs was clearly directed to other stated purposes, i.e., obtaining isoform-specific amplification. Thus, it should be clear that the selected primer pairs were incorporated for use into a type of standard PCR protocol, in which experimental samples are subjected to certain temperatures for certain time intervals, regardless of the particular nucleotide sequence of the primers. The oligonucleotide sequences of the primer pairs were not specified or identified on the basis of any particular annealing temperature, nor on the basis of any other particular temperature. In fact, as shown in the results of Fig. 8, and as further discussed in the descriptive caption accompanying the same, the authors did not fully accomplish or demonstrate differential expression of the two isoforms. According to their explanatory hypothesis, the avidity of binding for the primers specific to the full-length isoform may have been substantially greater than the binding avidity for the primers specific to the deletion isoform.

Thus, the authors clearly did not intend to specify the sequence of their primer pairs with a particular purpose of providing a positive control to obtain maximal annealing at some predetermined temperature, or in conformance with some predetermined annealing temperature. In fact, as their results show, their two sets of primers demonstrated distinctly different degrees of annealing. That is, the two primers exhibited clearly different efficiencies of annealing during a series of PCR reactions wherein the annealing temperature was held constant and invariant, according to the standard methodology of the PCR protocol described. Thus, it cannot be said that the primers were chosen or identified for their having a similar, or even approximately similar, annealing behavior, at the annealing temperature of the PCR protocol described.

(2) In the continued rejection, the Examiner suggests that Hwang et al. discloses that primer pair data must fail to match the gene family data. Again, the Applicant

respectfully disagrees with the Examiner's interpretation and rejection of claims 1 and 15 and submits that such claims are allowable for the following reasons.

Claims 1 and 15 recite "the set of primer selection rules including a second rule specifying that, based on a comparison of the primer pair data and gene family data of the gene sequence stored in a file, the primer pair data for the coding sequence must fail to match the gene family data." As described, the primer selection rules are rules that are followed by a computer in identifying primer pair data for each coding sequence. The specification is consistent with the claim interpretation that, with use of such a rule, a comparison is performed between primer pair data and gene family data and, if there is a match, the primer pair data are not obtained as primer pair data for the coding sequence. See e.g. the application on page 41 at lines 3-5: "[t]he primerout file lists candidate primer sequences that otherwise met the primer selection rules, but was found in one of the gene family files and was therefore rejected"; and on page 33 at lines 10-14: "[t]hus, the software can select primers that are unique to the gene of interest and can be relied upon for genes that are members of families. This functionality can be added to the functionality of picking the best primers around the exons of a gene for the primer design process – select the candidate primer only if it is unique to the target file and not present in the gene family files"). Hwang et al. teach or suggest nothing that remotely resembles the same.

For the reasons in (2) alone, Hwang et al. do not teach or suggest the invention as claimed and the Examiner's continued § 102(b) rejection should be withdrawn.

Further, in the previous Office Action of 3 November 2004, the Examiner directed the Applicant's attention to p. 3349 at the paragraph bridging cols. 1-2, and describes that Hwang et al "found a 3'-primer that did not match the gene family data of PLP-Cβ genes, which allowed him [sic] to only amplify one isoform," which does not teach or suggest what is claimed. In Hwang et al., the two separate 3'-primers that were synthesized for purposes of PCR amplification were substantially similar, having an overlapping region comprising ten consecutive nucleotides. However, it is evident that the strategy for selection of nucleotides in construction of the primer pairs was

determined entirely by the sequence of the primer target regions, the nucleotide sequences proximate to the 5' and 3' opposite ends of the segment to be amplified. These sequences were not so much chosen as they were required, as a matter of necessity, for purposes of obtaining amplification using a type of standard experimental protocol that is well known in the art. It is of course true that the two pairs of primers were not identical; however, the reason for this fact is not attributable to an intentional introduction of dissimilarity. In fact, it might have been entirely possible that the 5' primer and one 3' primer might have shared identical similarity of sequence, had their hybridization target regions also been identical. While the two 3' primers were constructed to be dissimilar, this fact cannot be said to have resulted from any particular intention or concern of the authors to apply two distinctly different primers. Rather, their dissimilarity was entirely defined within the purpose of the PCR protocol, to obtain differential expression of the two slightly dissimilar isoforms. Furthermore, an experimental protocol designed to differentiate between two isoforms of the same protein is not conceptually equivalent with differentiating between different members of a gene family. According to the generally accepted and conventional definition, the meaning of the latter term implies a multiple grouping of two or more distinctly separate genes, derived either from distinctly separate chromosomal locations within one genome, or indeed from entirely distinct biological species.

(3) In the continued rejection, the Examiner interprets the term "individual" as individual strands of nucleic acid, so that "three or more individuals" is interpreted as three or more strands of nucleic acid. Again, the Applicant respectfully disagrees with the Examiner's interpretation and rejection of claims 1 and 15 and submits that such claims are allowable for the following reasons.

The Applicant respectfully submits that the Examiner's interpretation of the term "individual" is not a reasonable interpretation. The claim term "individual" cannot be so broadly construed as to merely define an individual strand of nucleic acid. A plain and ordinary meaning (and even common sense meaning) of the term "individual" cannot

justify the Examiner's interpretation. Simply put, the limitation "three or more individuals" means three or more different people as provided in the present application.

The claim limitations must be interpreted in light of the specification. In the present case, the specification is inconsistent with the Examiner's interpretation but consistent with the Applicant's. In the specification, the term "individual" refers to a unique person so that "three or more individuals" refers to three or more different or unique people. See e.g. the present application in the following areas, e.g. on page 4 at lines 17-18: "Furthermore, one must first amplify regions of the human genome from *many different people* before comparing the sequences to one another"; on page 12 at lines 10-13: "In particular, the plurality of coding sequences in gene sequences from *three or more individuals (typically 100s of individuals)* are simultaneously amplified in a gene amplification machine at the predetermined annealing temperature using the identified pairs of primer sequences (step 314)"; on page 15 at lines 14-16: "The object of the present invention is to survey the coding sequences at each coding region for a given gene *in many different people*, which is time consuming and expensive using conventional approaches"; on page 42 at lines 6-8: "It is more efficient to do simultaneous amplifications of four or five regions *in 500 people*, for example, rather than doing them one by one." Further, dictionary definitions recite that the term "individual" means "a single human considered apart from a society or group", and "a human regarded as a unique personality," and even as "a single animal or plant as distinguished from a species, community, or group."

For the reasons in (3) alone, Hwang et al. do not teach or suggest the invention as claimed and the Examiner's continued § 102(b) rejection should be withdrawn.

Further, in the previous Office Action of 3 November 2004, the Examiner directed the Applicant's attention to p. 3346 at col. 2 and p. 3349 at the paragraph bridging cols. 1-2, which does not teach or suggest what is claimed. In this rejection, the Examiner specifically stated that, in Hwang et al., "three or more strands of DNA ... is present after the initial PCR amplification of PLP-Cβ." The following remarks are provided assuming the term "individual" is construed in a reasonable fashion, in

accordance with the specification. Regarding Hwang et al., the presumption of "three or more strands of DNA [being] present after the initial PCR amplification" is unfounded to the extent that only two strands might be present after the first PCR cycle, if only one strand of cDNA is present in the sample, to begin with. There is no proper presumption in any PCR amplification that even one double helix might in fact exist in the experimental sample. It is equally plausible to suppose that PCR might amplify one strand, separated away from one double-helical molecule of DNA, as to suppose that a given experimental sample might contain two, or three, or any other number of target strands. The entire purpose of the PCR methodology is to provide a suitable environment for such amplification to occur, using a reaction buffer containing sufficient primers and enzyme, and a sufficient supply of monomer nucleotides, such as to facilitate expansion of even the slightest trace of the target DNA. Further, it cannot be said that the cited publication provides an example of where PCR amplification was simultaneously conducted on samples of DNA obtained from three or more individuals. The amplified cDNA may have been from derived from one individual, one experimental animal, per each amplification. Similarly, amplification of cDNA obtained from mRNA samples harvested from tissue may very likely have involved a particular sample of mRNA from one experimental animal, or indeed might have been derived from one tissue slice, per each amplification.

In the same Final Office Action, the Examiner further failed to identify any repetitive computer process which executes the first and the second primer selection rules as claimed in claim 1. Put another way, Hwang et al. fail to teach or suggest a computer process which executes the first primer selection rule and the second primer selection rule as claimed.

In the same Final Office Action, the Examiner maintained rejection of claims 15, 19, and 20-22 under 35 U.S.C. § 103(a) as being unpatentable over Hwang et al.

Although the Applicant disagrees with the Examiner's rejections with respect to these claims, such rejections are moot in light of Applicant's arguments presented above.

Based on the above remarks, the Applicant respectfully requests reconsideration and allowance of all pending claims 1-3, 5-17, and 19-28 over the prior art of record. Since claims 1-3, 5-17, and 19-28 are allowable over the prior art of record, and no further issues remain, the Applicant respectfully submits that the application is now in a condition suitable for allowance.

Thank you for your reconsideration. Please feel free to contact the undersigned for any reason if it would expedite the prosecution of the present application.

Respectfully Submitted,

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JOHN J. OSKOREP
Reg. No. 41,234

JOHN J. OSKOREP, ESQ.
ONE MAGNIFICENT MILE CENTER
980 N. MICHIGAN AVENUE, SUITE 1400
CHICAGO, ILLINOIS 60611

Telephone: (312) 222-1860 Fax: (312) 214-6303